REMARKS/ARGUMENTS

Pending Claims

Claims 1-10 have been examined. Claims 11-32 have been withdrawn from consideration. Claim 1 has been amended. Support for amendments to the claims is provided, for example, in Fig. 1 and the explanation of Fig. 1 on page 16, line 8 to the bottom of the page of the specification. Also see, for example, page 10, line 4 from the bottom to the last bottom line of the specification. No new matter has been added.

Sequence Compliance

The application has been objected to for some sequences not containing a SEQ ID NO. Particularly, sequences shown on pages 9, 10, and 21 of the present specification have been objected to. The specification has been amended to incorporate sequence numbers for those sequences that did not contain a SEQ ID NO. See Amendments to the Specification. Furthermore, a corrected computer readable sequence listing with the new sequence numbers (SEQ ID NOs 26-31) is provided with this response. Claims 22 and 23 were not amended because they were withdrawn from consideration. No new matter has been added. Withdrawal of this objection is respectfully requested.

Claim Rejections – 35 USC §103

Claims 1-10 have been rejected under 35 USC §103(a) as being unpatentable over Schakowski et al. (Molecular Therapy, vol. 3, No. 5, May 2001, pages 793-800), in

view of Taki et al. (Nucleic Acid Research Supplement No. 3, 191-192, 2003, Oxford Press), and Scherr et al. (Cell Cycle, 2:3, 2003, pages 251-257). Applicant respectfully traverses the §103(a) rejection for at least the following reason.

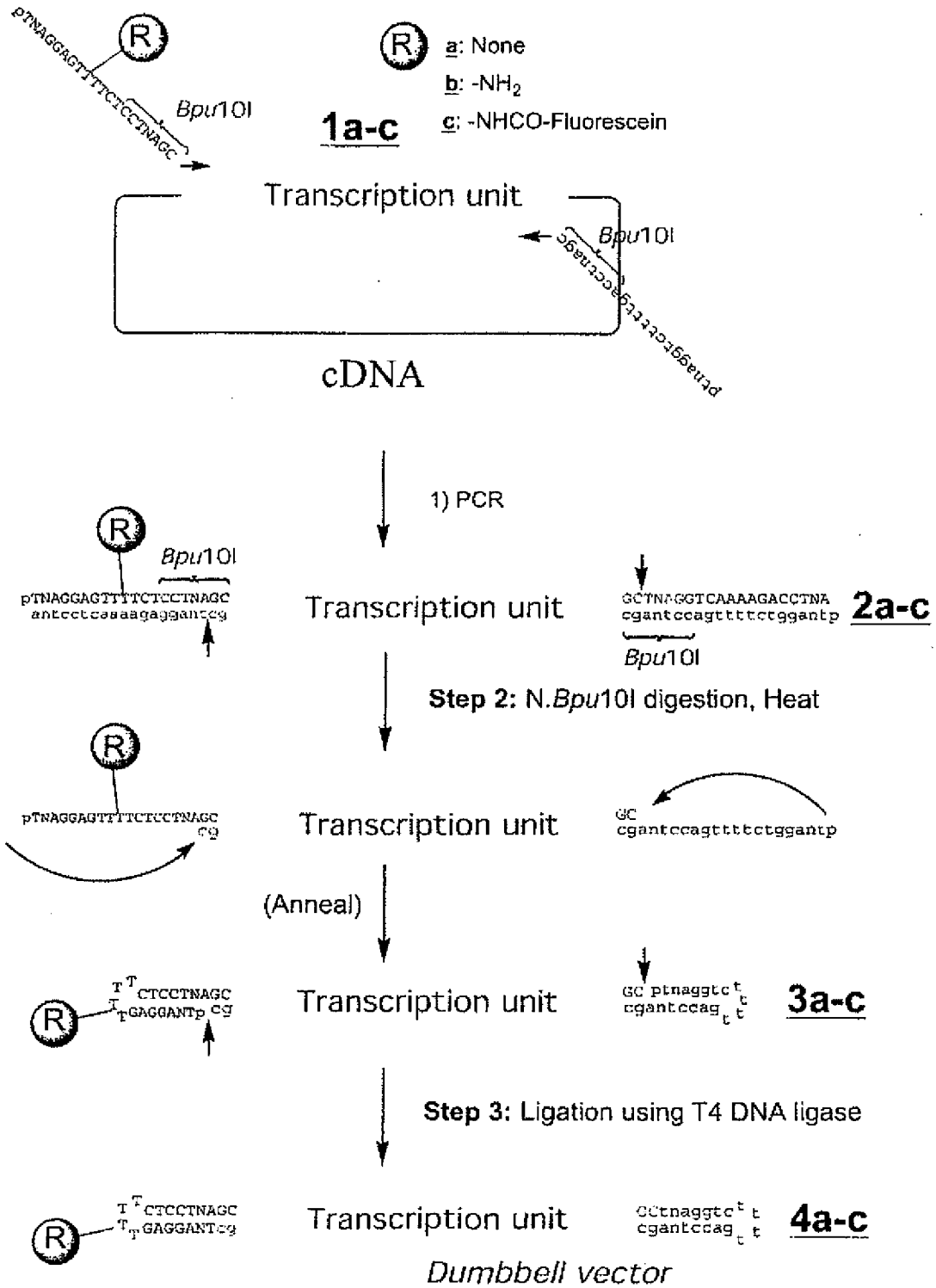
Claim 1 recites as follows:

> Claim 1 (currently amended): A method for producing a dumbbell-shaped DNA, wherein each of sense and antisense strands is connected at both the 5' and 3' ends of a linear-shaped double stranded DNA by a single stranded DNA ~~of~~ loop structure, comprising the steps of:
>
> 1) amplifying a target DNA in a template DNA by PCR using sense and antisense primers attached to the target DNA, wherein each of the sense and antisense primers contains the following sequence (a) at the 5' end and also contains the following sequences (b), (c), and (d) in order from the 5' end to the 3' end, (a) a part of a sense sequence of a nickase recognition sequence, comprising the sequence of a region between the site where a nick is introduced by the action of a nickase, and the 3' end, (b) a sequence capable of forming a loop structure from a single strand, (c) the entire antisense sequence of the nickase recognition sequence (a), (d) a sequence complementary to all or part of the sequence of the target DNA;
>
> 2) treating the amplified DNA product of step 1) with a nickase of (a);
>
> 3) heating and then annealing the nickase treated amplified DNA product of step 2); and
>
> 4) treating the heated and annealed amplified DNA product of step 3) with DNA ligase, wherein the sense and antisense primers used in step 1) are phosphorylated at the 5' end, or the amplified DNA product is phosphorylated at the 5' end after step 1) but before step 4).

Claim 1 recites an invention where that the loop structure that is to be formed is already attached to the target DNA so that modification/ligation to form a loop is executed intramolecularly. That is, as stated in step 1), a target DNA is amplified in a template DNA by PCR using sense and antisense primers attached to the target DNA. The attached sense and antisense primers separately contain a part of a sense sequence of a nickase recognition sequence at the '5 end, and furthermore, a sequence

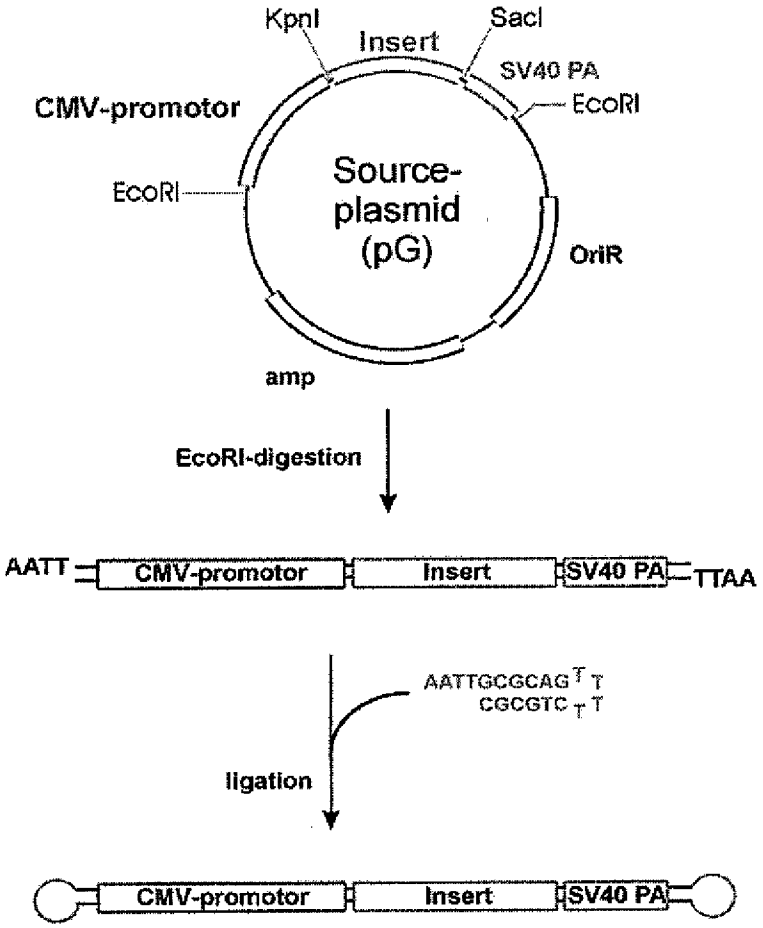
capable of forming a loop structure from a single strand, the entire antisense sequence of the nickase recognition sequence, and a sequence complementary to all or part of the sequence of the target DNA in order from the 5' end to the 3' end. When the amplified DNA is treated with a nickase, heated, annealed, and then ligated, a dumbbell-shaped DNA product is produced intramolecularly. That is, no external molecules are brought in to attach to the DNA to form a dumbbell-shaped DNA at these steps. An example of the invented method where a dumbbell-shaped DNA is made intramolecuarly is shown in Fig. 1 of the present specification.

Fig. 1


a: None
b: -NH2
c: -NHCO-Fluorescein
1a-c
Bpu10I
Transcription unit
cDNA
1) PCR
2a-c
Step 2: N.Bpu10I digestion, Heat
3a-c
(Anneal)
Step 3: Ligation using T4 DNA ligase
4a-c
Dumbbell vector

The Example above shows a transcription unit attached to the primers. The amplifying, nicking, heating, annealing, and ligating steps on the DNA to produce the Dumbbell-shaped DNA are executed intramolecularly in that no external oligodesoxynucelotides are added to ligate to the DNA produce the dumbbell-shaped DNA.

On the other hand, Schakowski shows a conventional intermolecular ligation step to form the dumbbell-shaped DNA. This is clear from Fig. 1 which shows a 20-mer hairpin oligodeoxynucleotides (ODN), AATTGCGCAGTTTTCTGCGC, being ligated with the target DNA.



Also, the explanation on Fig. 1 states that the ODN, which is the dumbbell loop structure, has to be added in 80-fold molar excess in relation to plasmid units to avoid vector multimerization (see page 795, first column). The present invention can more efficiently produce the dumbbell DNA then by the process described in Schakowski because the loop structure is formed intramolecularly rather than intermolecularly. In the present invention, there is no need to add oligodesoxynucelotides in80-fold molar excess to produce the dumbbell-shaped DNA. Thus, it is clear that Schakowsky does not disclose, teach or suggest the method as set forth in the present claims.

Taki et al. lists the following authors: Masumi Taki, Yoshio Kato, Makoto Miyagishi, Yasuomi Takagi, Masayuki Sano, and Kazunari Taira. With the exception of Masayuki Sano, all are named inventors of the present application. Attached herewith is a disavowing declaration from Masayuki Sano that relevant portions of Taki et al. originated with or obtained from at least one of the named inventors of the present application. That is, Masayuki Sano is not the inventor of the invention set forth in the pending claims. The remaining authors -- Masumi Taki, Yoshio Kato, Makoto Miyagishi, Yasuomi Takagi, and Kazunari Tairo -- are the same named inventors of the present application. Therefore, the disclosure of Taki et al. was derived from the named inventor(s) own work.

To establish that Taki et al. is not time barred within the meaning of §102(b), a cover page of Nucleic Acids Research Supplement No. 3, which contained Taki et al, is provided with this response as Exhibit A. This cover page verifies that Taki et al. was published on or around September 17, 2003. The Japanese priority application was

filed on August 8, 2003. The PCT application, which claims the benefit of this Japanese priority application and has designated the US, was filed on August 9, 2004. The present application entered into the US national stage based on this PCT application. Thus, Taki et al. was published within a year before the filing of Applicant's PCT application. Applicant is not time barred within the meaning of §102(b) to remove Taki et al as a reference. See MPEP 2132.01.

Therefore, for at least the foregoing reason, Taki et al. is removed as a prior art reference against the present application.

No comment is made with regard to Scherr et al. because Applicant is believed to have overcome the §103 rejection based on the submission that Schakowski is patentably distinct from the method as set forth in the pending claims and that Taki et al. is removed as a reference.

For at least the foregoing reasons, claims 1-10 are not obvious over Schakowski et al. (Molecular Therapy, vol. 3, No. 5, May 2001, pages 793-800), in view of Taki et al. (Nucleic Acid Research Supplement No. 3, 191-192, 2003, Oxford Press), and Scherr et al. (Cell Cycle, 2:3, 2003, pages 251-257).

Summary

The application is believed to be in condition for allowance. If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
HOGAN LOVELLS US L.L.P.

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